COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

© 2019 EDIZIONI MINERVA MEDICA
Online version at http://www.minervamedica.it

Minerva Anestesiologica 2020 March;86(3):327-40
DOI: 10.23736/S0375-9393.19.13852-7

EXPERTS' OPINION

How to use cerebral ultrasound in the ICU

Rita BERTUETTI [1], Paolo GRITTI [2], Paolo PELOSI [3], Chiara ROBBA [4] *

[1]Department of Anesthesia, Intensive Care and Emergency Medicine, Spedali Civili University Hospital, Brescia, Italy; [2]Department of Anesthesia and Critical Care Medicine, Papa Giovanni XXIII Hospital, Bergamo, Italy; [3]Department of Surgical Sciences and Integrated Diagnostics, University of Genoa, Genoa, Italy; [4]Department of Surgical Sciences and Integrated Diagnostics, San Martino University Hospital IRCCS, University of Genoa, Genoa, Italy

*Corresponding author: Chiara Robba, Department of Surgical Sciences and Integrated Diagnostics, San Martino University Hospital IRCCS, University of Genoa, Largo Rosanna Benzi 15, 16100 Genoa, Italy. E-mail: kiarobba@gmail.com

ABSTRACT

Cerebral ultrasound is a developing point of care tool for intensivists and emergency physicians, with an important role in the diagnosis of acute intracranial pathology, such as the assessment of cerebrovascular diseases and in the noninvasive intracranial pressure measurement both in the acute clinical settings and in intensive care unit (ICU). The traditional application of transcranial doppler (TCD) by assessing blood flow velocities in the main cerebral arteries, allows the evaluation and follow up of cerebral vasospasm, cerebral perfusion pressure, cerebral autoregulation and intracranial hypertension. The use of TCD, traditionally limited to the neurosonology laboratories settings, has expanded over the last years following the introduction of B-mode ultrasound and color Doppler, the transcranial color-coded duplex ultrasonography (TCCS), opening a new window to the assessment of cerebral anatomy not only in the neurocritical patients, but also in general ICU and emergency room patients. Here we report a brief review with the intent to up-to-date and describe the main applications and use of TCD/TCCS in the setting of Neurointensive Care.

(*Cite this article as:* Bertuetti R, Gritti P, Pelosi P, Robba C. How to use cerebral ultrasound in the ICU. Minerva Anestesiol 2020;86:327-40. DOI: 10.23736/S0375-9393.19.13852-7)

KEY WORDS: Brain injuries; Ultrasonography, Doppler, transcranial; Intensive Care Units.

The first historical use of ultrasound for the evaluation of the brain was performed in 1942 by Karl Theodor Dussik, in Austria, who published his technique in 1942 with the name of "Hyperphonography of the Brain."[1] However, in 1952, Guttner *et al.* showed that the transmission method was of no value because of the great absorption and reflection of the ultrasonic waves by the bone structure in the cranium.[2] In the following years, transcranial echography was in part abandoned until the end of 1970s when two-dimensional B-mode imaging was applied to visualize through the fontanels the cerebral parenchyma in young children.[3] After Aaslid development of transcranial doppler (TCD) sonography for the examination of cerebral hemodynamics in 1982,[4] high-resolution ultrasonic systems and high performance sector transducers have opened up new perspectives for transcranial examination in adults.[5] Despite technical difficulties at the beginning of the transcranial color-coded duplex ultrasonography (TCCS) period, during the last two decades TCCS found its important role in the diagnosis of intracranial space occupying lesions and assessment of intracranial pressure, intracranial hemorrhage, hydrocephalus, midline shift and cerebrovascular diseases in both acute and chronic clinical settings.[6-8] TCCS not only allows visualization of brain parenchymal structures but through the color Doppler mode allows direct identification of the vessels course and pulsed Doppler angle correction

SHOUT
SHARE
IT

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

TABLE I.—*Anatomical landmarks and normal velocity values of TCD and TCCS.*[8-10]

Windows	Position	TCD depth and setting	Vessels	Depth
Transtemporal insonation	Above the zygomatic arch and aim it slightly upwards and anterior to the contralateral ear/ window	Initial set 50-56 mm Range 30-75 mm	MCA ACA MCA/ACA PCA, P1 PCA, P2 TICA	30-60 mm 60-80 mm 60-65 mm 60-70 mm 60-70 mm 55-65 mm
Transorbital insonation	Place the transducer over eyelid and angle it slightly medially.	Decrease power to minimum. Set the depth at 50-52 mm. Range 40-80 mm	OA CS	40-60 mm 60-80 mm
Suboccipital insonation	Place the transducer at midline an inch below the edge of the skull and aim it at the bridge of the nose	Set the system back to full power. Set the depth at 75 mm (presumed location of both terminal VAs and proximal BA).	VA BA	60-90 mm 80-120 mm
Submandibular insonation	Laterally under the jaw anterior and medial to the sternocleidomastoid. Aim the transducer upwards and slightly medially.	Set the depth at 50 mm. Range 30-50 mm	ICA	40-50 mm

MCA: middle cerebral artery; ACA: anterior cerebral artery; PCA: posterior cerebral artery; P1: first segment of the posterior cerebral artery; P2: second segment of the posterior cerebral artery; TICA: terminal internal carotid artery; CS: carotid Siphons; VA; vertebral artery; BA: basilar artery; ICA: internal carotid artery.

which allows a more precise estimation of flow velocities especially when insonation angles are >30° (Table I, Figure 1).[8-14]

Intracranial hypertension

Intracranial hypertension (IHT) and reduced cerebral perfusion pressure represent well known fearful complications in many types of acute brain injuries. Brain ultrasound can provide valuable information about intracranial pressure (ICP) and cerebral perfusion pressure (CPP) especially when different ultrasound-based techniques are integrated. Several ultrasound based techniques for the evaluation of ICP have been studied: TCD or TCCS and the analysis of flow velocity waveform variations in the middle cerebral artery (MCA) and straight sinus (SSV); measurement of the optic nerve sheath diameter (ONSD); evaluation of midline shift (MLS).

Analysis of flow velocity waveform variations

Variations in ICP affect blood flow velocity in major cerebral vessels. Since the MCA behaves as a biological pressure transducer for the brain, its compliance and transmural pressure represent the main variables affecting the flow velocity (FV) of the blood. Cerebral arteries surrounded by the brain parenchyma enclosed in the skull behave as a Starling resistor so that when ICP raises a fall in diastolic cerebral blood flow velocity (diastolic FV), a peaked waveform, and an increase in Pulsatility Index (PI) are typically observed (Figure 2).[15, 16]

The Gosling PI: systolic FV- diastolic FV/ mean FV, is based on the changes that take place in the TCD waveform when the intracranial hemodynamic modifies. PI reliability in assessing ICP has been tested by different authors, although absolute accuracy seems to be too poor, and ability in discriminating critical cut off not reliable enough (Table II).[13, 17-31]

Different formulas and mathematical approaches have been proposed for ICP and CPP estimation. Aaslid *et al.* firstly presented a formula for the estimation of CPP, based on Spectral Pulsatility Index (SPI) and the first harmonic component of the arterial blood pressure (ABP) which demonstrated to be quite sensitive to the variation of CPP, but limited in accuracy.[21] Few years later, Czosnyka *et al.* proposed and validated a new non PI-related formula for estimation

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

Directions	TCD Mean Velocities	TCCS planes and main structures
Towards	55±12 cm/sec	Transtemporal insonation allows visualization of the basal structures at the base of the brain and the cerebral arteries at the level of the circle of Willis.
Away	50±11 cm/sec	
Bidirectional	39±10 cm/sec	Mesencepalic plane:
Towards	40±10 cm/sec	It allows identification of the contralateral skull and the midbrain, usually easily identified at the midline, and it resembles a butterfly with the wings directed anteriorly.
Away	39±10 cm/sec	
Towards		Diencephalic plane:
		From the mesencephalic plane, an approximate 10° cranial tilting of ultrasound beam allows identification of the third ventricle, seen as two pulsating parallel lines positioned slightly more cranial and anterior to the midbrain.
		Ventricular plane:
		Further cranial tilting of the ultrasound beam allows visualisation of the thalami and frontal horns of the lateral ventricles.
Towards	21±5 cm/sec	Transorbital plane: insonation through the closed eyelid allows visualization of the ophthalmic artery and the carotid siphon, as well as of the optic nerve sheath.
Bidirectional	45±15 cm/sec	
Away	38±10 cm/sec	Suboccipital plane: this approach allows visualization of the foramen magnum and the distal segment of the vertebral arteries and of the basilar artery.
Away	41±10 cm/sec	
Away	37±8 cm/sec	Submandibular plane: this approach can be used to insonate the extra-cranial portion of the internal carotid artery (ICA) to calculate the mean flow velocity ratio between middle cerebral artery and the ICA (Lindegaard Index).

of CPP — and therefore ICP — which proved to have a good accuracy compared with the gold standard in terms of CPP estimation, despite not being precise enough for ICP.[22] A different point of view for clinical application of the mentioned formula is provided in a recent study (IMPRESSIT) where the elevated negative predictive value of the formula in ruling out ICH has been recently reinforced: in all the collected cases, patients with a low nICP had also low invasive (measured) ICP.[23] More complex and elegant methods are described in literature, being such methods, though, confined for research only as still too sophisticated for daily clinical application (Table II).[24-26, 32]

Venous TCD finds its application in diagnosis and follow-up of outcomes in cerebral venous thrombosis, stroke, and head trauma. The straight sinus identification is based on the occipital probe position directed upwards and towards the brain midline, a signal direction towards the probe at an insonation depth 50-80 mm.[33] The first systematic transtemporal insonation of the basal vein of Rosenthal (BVR) was performed using TCD vessel can be identified in proximity of the P2-segment of the PCA. TCD detection rates range from 78% to 100% (Figure 3).

Serial venous TCD studies of the BVR and the straight sinus (SSV) explore the relationship between ICP and gPI derived from venous flow velocities (maximal BFV - minimal BFV)/mean BFV); as a result, linear relationship between mean ICP and maximal venous BFV in the basal vein of Rosenthal (r=0.645; P=0.002) and in the straight sinus has been observed (r=0.928; P=0.0003). One of the limits of the technique is that the insonation of the basal vein of Rosenthal is only achievable in 88% of and the straight sinus in 72% of the patients.[34]

ONSD

The sheath enclosing the optic nerve is in direct continuity with the dura mater and the CSF-containing subarachnoid space of the brain and, since the ONS is distensible, CSF pressure variations influence the volume of ONSD particularly in the anterior, retro-bulbar compartment, about 3 mm behind the globe (Figure 4). Whenever ICP raises, subarachnoid compartment of the nerve is also affected, the optic nerve sheath is thus stretched resulting in an enlargement of

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

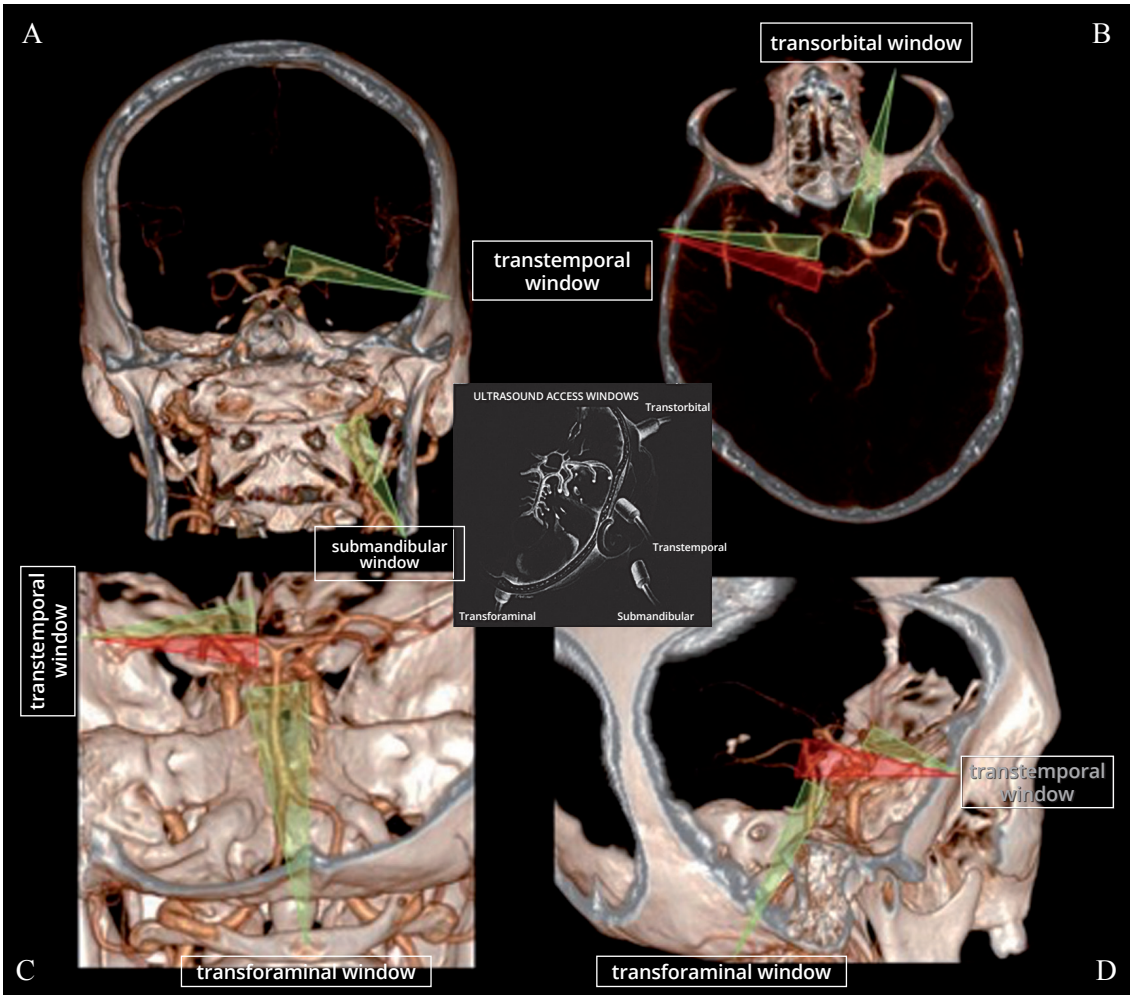

Figure 1.—A-D) Views of skull and the main arterial vessels with the four common acoustic windows used in transcranial Doppler examination (triangle). Transtemporal window, submandibular window, transorbital window, suboccipital or transforaminal window. The transtemporal approach allows velocity measurements in the middle (MCA), anterior (ACA), posterior (PCA) and communicating arteries (A-D). The transorbital approach is used to insonate the ophthalmic artery (OA), the internal carotid artery (ICA) siphon and the optic nerve sheath (B). The suboccipital approach allows insonation of the terminal vertebral (VA) and basilar (BA) arteries through the foramen magnum (C, D). The submandibular window (A) can be used to insonate the extra-cranial portion of the internal carotid artery to calculate the Lindegaard Index. To note the angle of the posterior cerebral artery respect to the median cerebral artery and the communicating anterior cerebral artery. views of skull and the main arterial vessels with the four common acoustic windows used in transcranial doppler examination (triangle). The transtemporal approach allows velocity measurements in the middle (MCA), anterior (ACA), posterior (PCA) and communicating arteries (A-D). The transorbital approach is used to insonate the ophthalmic artery (OA), the internal carotid artery (ICA) siphon and the optic nerve sheath (B). The suboccipital approach allows insonation of the terminal vertebral (VA) and basilar (BA) arteries through the foramen magnum (C, D). The submandibular window (A) can be used to insonate the extra-cranial portion of the internal carotid artery as much close to the carotid canal in order to calculate the Lindegaard Index. To note the angle of the posterior cerebral artery respect to the median cerebral artery and the communicating anterior cerebral artery.[8-14]

the optic nerve sheath diameter.[35] Scientific literature describes a linear relationship between peri-optic CSF pressure and ICP; in fact, ONSD increases almost directly with ICP, as during osmotic therapy or following CO_2 variations.[36, 37] Ultrasound (US) based ONSD measurements is used to evaluate intracranial hypertension in a binary mode, at such purpose literature provides many studies where ONSD has been compared with gold standard ICP monitoring in order to find cut-offs and accuracy. Reported cutoff values for normal ICP (ICP≤20 mmHg) assessed

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

TABLE II.—*Different TCD/TCCS based techniques for estimation of ICP.*[13, 17-30]

Method	Type of study, accuracy & iICP	Sensitivity	Specificity	AUC
PI = (FVs-FVd)/FVm	Correlation PI- iICP ranges from R=0.22 (Behrens *et al.*)[18] to 0.94 reported in Bellner *et al.* study.[17] Zweifel[19] also reports a poor correlation with a wide prediction interval (> ±15 mmHg). Bouzat *et al.*[20] in a study on moderate TBI found a correlation between PI>1.25, low FVd (<25 cm/sec) and neurological deterioration.	Threshold 20 mmHg: 83% (Bellener *et al.*)[17] 80% (Bouzat *et al.*)[20]	Threshold 20 mmHg: 99% (Bellner *et al.*);[17] 79% (Bouzat *et al.*)[21]	0.62 (ICP≥15 mmHg) 0.74 (ICP≥35 mmHg) (Zweifel *et al.*)[19]
nICP Aaslid: nCPP =A1 *FVm/FV1 nCPP according to Aaslid Formula is derived from the relationship between the first harmonic component of the pressorial pulse (A1) and SPI (SPI is obtained by the first harmonic component of flow velocity pulsation (FV1), divided by the FVm (SPI =FV1/FVm))	Aaslid *et al.*[21] found SD for nCPP estimation of 8.2 mmHg at 40 mmHg. Good ability in differentiation between low (<40 mmHg) and normal (>80) CPP Experimental study on infusion study in rabbits, Robba *et al.*[29] found a correlation nICP and ICP was R=0.53			
nICP_FVd nCPP= FVd/FVm * MAP +14	Czosnyka *et al.*[22, 30] describe a new method/formula for nCPP estimation (and then nICP) based on TCD flow velocity and MAP. Correlation nCPP- CPP R=0.73 Estimation error was less than 10 mmHg in 71% and less than 15 mmHg in 84% of cases. Schmidt *et al.*[30] evaluated nICP_FVd *vs.* iICP: error for nCPP estimation was less than 10 mmHg in 89% and less than 13 in 92% of a cases. Correlation between nICP_FVd-iICP according to Robba *et al.*[29] is R= 0.77. Reliability of this formula in excluding ICH is very high (Rasulo *et al.*)[23]	100% (Rasulo *et al.*)[23]	91% (Rasulo *et al.*)[23]	0.86 for nICP≥20 mmHg 0.94 for nICP≥40 mmHg (Robba *et al.*)[29] 0.96, best threshold for nICP=24 mmHg[23]
nICP_BB method for nICP calculation based on FV and ABP using a black-box model	Schmidt *et al.*[24] describe and assess this new black-box method and comparison with iICP: mean absolute difference between nICP_BB and iICP of 4.0 mmHg and standard deviation of error of 1.8 mmHg. The same authors[25] evaluate nICP_BB during plateau waves of iICP in TBI and stroke patients. Correlation nICP_BB and iICP during ICP increases was R=0.98. Mean absolute difference of 8.3 mmHg and standard deviation of error 5.4 mmHg at baseline, during top phase of plateau waves, respectively, 7.9 mmHg and 4.3 mmHg In a more recent paper Cardim *et al.*[28] finds a correlation nICP_BB and iICP was R=0.39 bias -0.50±5.0 mmHg			0.66 (Schmidt *et al.*)[24]
nICP_Heldt mathematical algorithm based on cerebrovascular dynamics for nICP estimation based on FV and ABP (Kashif *et al.*)[26]		90%	80%	0.88 for ICP≥20 mmHg[26]
nICP_SSV	Linear relationship between mean ICP and maximal venous FV in the basal vein of Rosenthal (r=0.645; P=0.002) and in the straight sinus has been observed (r=0.928; P=0.0003).[31] Robba *et al.*[27] describe a mathematical relationship between maximal SS FV and iICP, positive correlation R=0.72	87% (Robba *et al.*)[27]	77% (Robba *et al.*)[27]	0.81 (0.74–0.87) (for maximal SS FV, Robba *et al.*)[27] best cut off for max SS FV 38 cm/sec (iICP>20 mmHg)

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

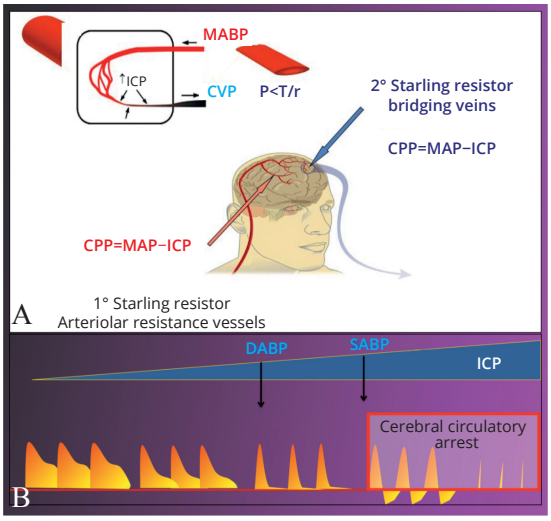

Figure 2.—Schematic representation of the behavior of cerebral vessels according to starling resistor theory (A); B) transcranial Doppler changes in middle cerebral artery (MCA) mean flow with progressive increase in intracranial pressure (ICP) The initial stage has a typical pattern of systolic peaks with progressive reduction in diastolic velocities.[15, 16]
P: pressure; T: wall tension; r: vessel radius; DABP: diastolic ABP; SABP: systolic ABP; CCP: critical closing pressure.

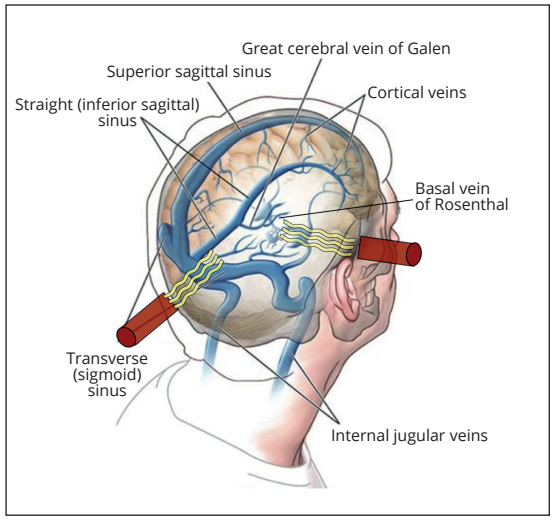

Figure 3.—Insonation technique of SSV and BVR.

with ONSD range from 4.8 to 6.3 mm.[38] A recent meta-analysis by Robba *et al.* including 275 patients has underlined the good diagnostic accuracy of ONSD in detecting ICH despite the heterogeneity either in the analyzed studied and in the cut off used; authors suggest the use of this diagnostic test in emergency setting and in situation when invasive monitoring is not available or eligible and call for more studies aiming to identify a clear cut off diagnostic value standardized for diverse subgroups categorized by age, gender, and condition.[39]

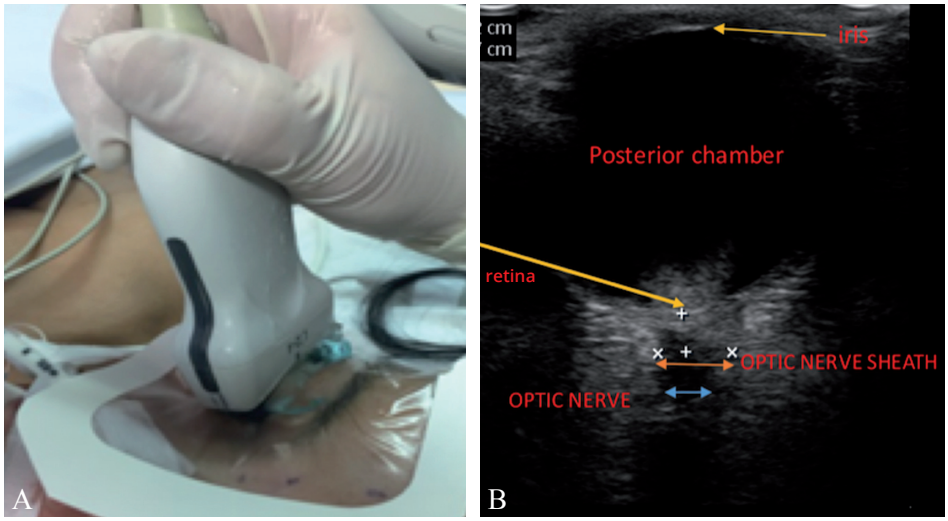

Figure 4.—ONS is insonated by genty placing a linear probe (7-10 Hz) on the upper lid, slightly on the temporal side: eye bulb is then visualized (iris and posterior chamber), optic nerve is an hypoechoic linear structure stretching perpendicularly to the probe, behind the optic disc/retina. ONS is slightly more echogenic: measure of the diameter is taken 3 mm behind the retina. Insonation of the ONS and measurement of ONSD should be attempted both in the cornal plane and sagittal plane. Attention must be payed to pit falls and artifacts: retinal artery can sometimes run around the nerve or the retina itself can cast a conical shadow behind the eye bulb mimicking an enlarged ONSD.

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

MLS

Brain MLS is a life-threatening complication of many acute brain injuries and calls for expeditious diagnosis and treatment. MLS is deemed significative when exceed 0.5 cm on head CT and predicts poor neurological outcome. Since brain ultrasound allows visualization of the third ventricle, this can be considered point of reference for midline structure in the sonographic anatomy. US-MLS compared to the gold standard determination shows a positive correlation with CT-MLS with a tendency to slightly underestimate the measure (Figure 5).[40]

Ultrasound based techniques for the estimation of ICP (nICP) have been recently studied in several clinical contexts. Cardim *et al.* in a cohort of hypoxic brain injured patients after cardiac arrest calculated non invasive ICP (nICP) using ONSD ($nICP_{ONSD}$) and $nICP_{FVd}$ (based on Czosnyka formula) yielding good results (ONSD and $nICP_{FVd}$: area under the receiver operating curve (AUC)= 0.96 [95% CI: 0.90-1.00] and AUC=0.91 [95% CI: 0.83-1.00], respectively).[41] Another field that has been lately gaining great interest, is the use of brain ultrasound for quick assessment of ICP in emergency room. Especially in major trauma victims, evaluation of encephalic injuries has been traditionally referred to head CT, so that in comatose patients with a Focused Assessment Sonography for Trauma (FAST) positive for intra-abdominal bleeding, any brain oriented evaluation and strategy was delayed until emergency surgery had been performed. Introduction of brain US into the FAST routine can potentially provide some information about presence of ICH by combined application of TCCS, ONSD and MLS and moreover, in some cases it can allow visualization of subdural or epidural hematomas and contusions. Such approach could prompt to a more brain oriented medical approach and, perhaps, joined general surgeon- neurosurgeon interventions.[42] Figure 6 shows integrated approach ONSD-flow velocity analysis for the evaluation of ICH.

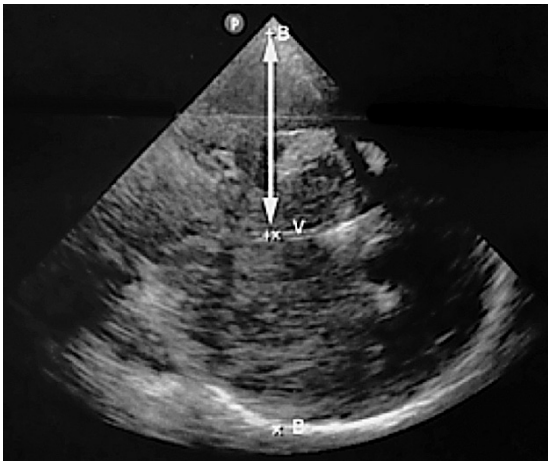

Figure 5.—Midline shift measurement. Ipsilateral and contralateral bone table and (B) the third ventricle, identified as a double hyperechogenic image over the midbrain (V). The distance between the external bone table and the center of the third ventricle is measured bilaterally (arrow).[40] MLS=(B1V-B2V)/2.

Vasospasm on TCD and TCCS in aneurysmal subarachnoid hemorrhage patients

Although representing only 3% of all strokes, aneurysmal subarachnoid hemorrhage (aSAH) remains one of the most devastating acute cerebral events with an incidence between 7.2 to 11.3 per 100.000 people per year.[43] Angiographic vasospasm and delayed cerebral ischemia are the most severe consequences in aSAH patients.[44] TCD and TCCS are both well-established methods to assess vasospasm in the acute phase after subarachnoid hemorrhage (SAH).[45] Sensitivity and specificity of TCD ultrasonography techniques regarding vasospasm vary widely depending on the analyzed intracranial artery and the different diagnostic criteria;[46, 47] however since its inception, the reliability of TCD ultrasonography in comparison with DSA is greatest in the M1 segment of the middle cerebral artery (MCA).[48] The diagnostic dilemma when using TCD for the assessment of vasospasm is the reliability of velocity thresholds; in fact, while an elevated cut off value (≥200 cm/sec for mean FV, Vmean) yelds to a specificity around 98% for MCA, sensitivity is negatively affected (27%) leading thus to a consistent number of false negative results. Literature has widely investigated this topic comparing TCD velocities with the gold standard examination for vasospasm, *i.e.* angiography, and a threshold

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

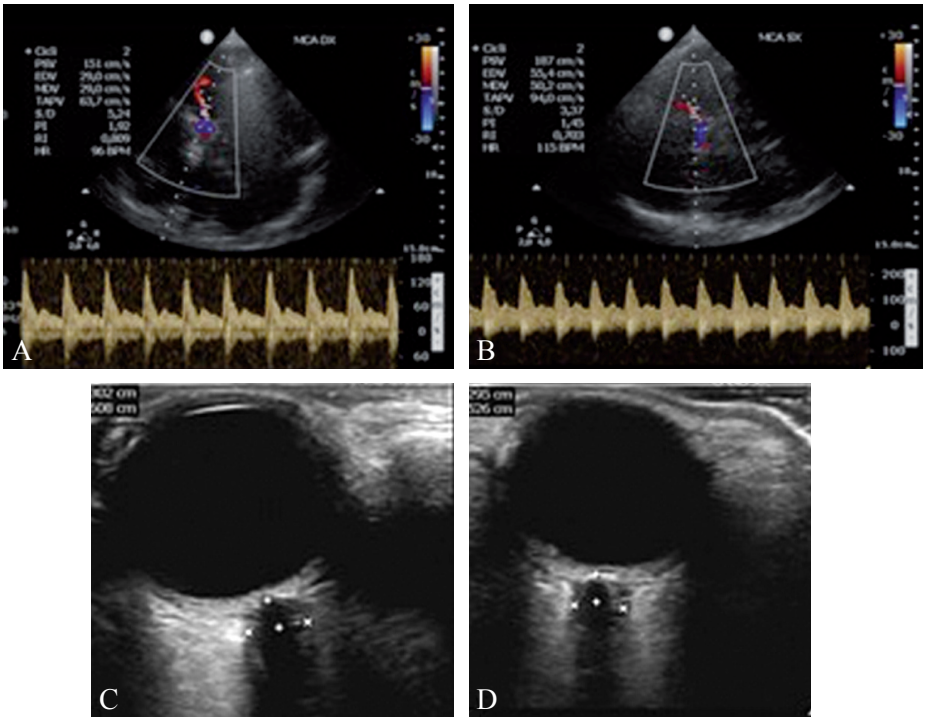

Figure 6.—A-D) Flow velocity in middle cerebral artery (MCA) and ONSD sonography of the same patient: before (A, C) decompressive craniectomy - showing typical intracranial hypertension waveforms alterations (increased PI, spiky waveform) and enlarged ONSD- and after decompressive craniectomy (B, D) where MCA flow velocity waveform shows an increased diastolic flow velocity and a smothered shape, ONSD is reduced as well.

value of ≥120 cm/sec (Vmean) seems to allow the best combination between sensitivity (88%) and specificity (72%).[9] However, increased velocity can be detected not only in cerebral vasospasm, but also in cerebral hyperperfusion or hyperemia: Lindegaard Index (Lindx), (MCA/internal carotid artery (ICA) ratio of the MCA FV to the ICA FV) is generally used for the differential diagnosis and might be a useful tool to discriminate between vasospasm and cerebral hyperperfusion using TCD ultrasonography, especially in patients with moderately increased in blood FV (Figure 7).[49]

The blood FV of the main venous vessel might reflect the cerebral blood flow (CBF), and patients with SAH and vasospasm with decreased blood FV in the basal vein of Rosenthal have worse clinical outcome.[50] The advent of TCCS enables the visualization of flow velocities in venous cerebral vessels. Recently, a new Intracranial Arteriovenous Index (AVI) between blood FVs in the MCA and the basal vein of Rosenthal was introduced to assess vasospasm after SAH (AVI>10 for mean velocity and an AVI>12 for systolic velocity indicates vasospasm) with a slightly higher reliability compared to the established Lindegaard Index and with lower failure rate.[51, 52]

Cerebral autoregulation

Cerebral autoregulation (CA) is the ability of the brain to maintain CBF constant despite changes in CPP. Dysfunction of CA has been observed in TBI, stroke, aSAH and carotid disease,[52-55] and it is associated with an increased risk of developing ischemia and cerebral edema. CA is classified in vasomotor reactivity, which is the response of the cerebral circle to changes in arterial partial pressure of carbon dioxide ($PaCO_2$) and arterial partial pressure of oxygen (PaO_2) and pressure type regulation, which preserves CBF from potential CPP changes, as long as the variations are within the mean pressure range of 50 and 150

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

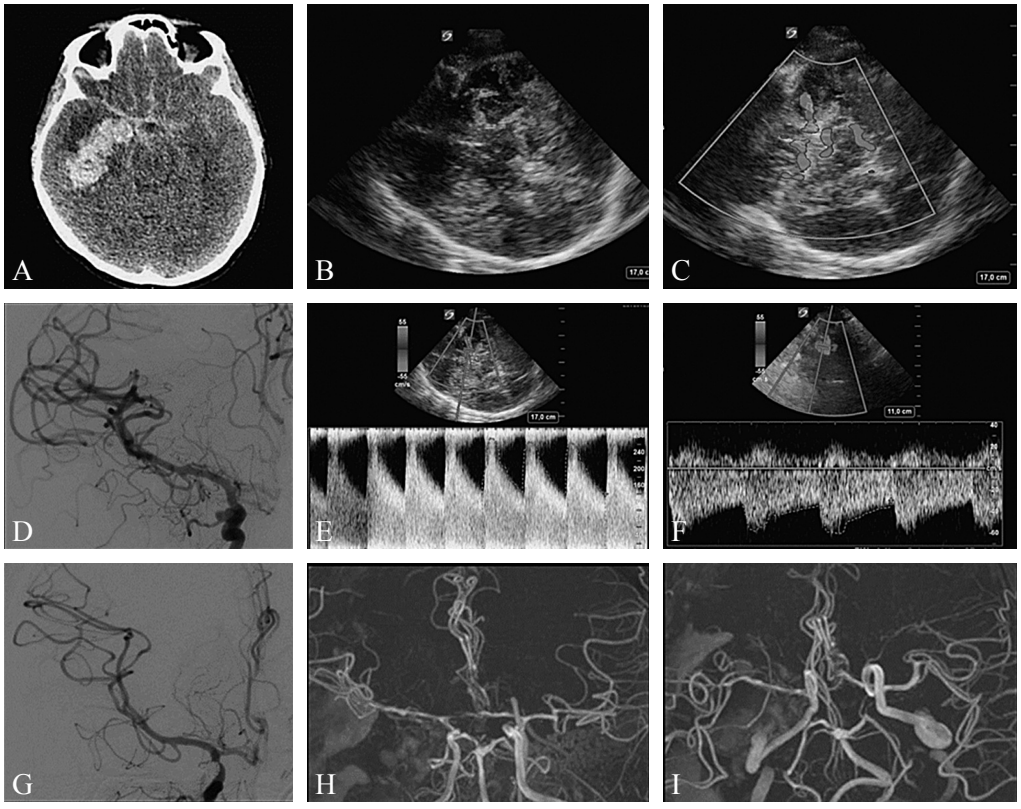

Figure 7.—A-I) Example of use of TCCS for vasospasm evaluation. Forty-five years old female underwent coiling for an ICA-Siphon aneurysm (panels A, D, G) and right decompression and hematoma evacuation. TCCS ultrasonography performed trough craniotomy show clearly mesencephalon and brain parenchyma (B) and a nearly complete Willis circle (C). Doppler exams showed an increase in velocity trough the right M1 mean cerebral artery (mean FV 203 cm/s) during the following days (H). It could be due also to the hyperemia and vascular low resistance in the right hemisphere caused by decompressive craniectomy. However an evaluation of ICA velocity of 45 cm/s and a consequent Lindegaard Index of 4.5 (F) suggestive for moderate vasospasm was subsequently confirmed by a 3d AngioMRI exam (H, I).[49]

mmHg. Pressure regulation can be further subdivided into dynamic regulation, involving a rapid accommodating response of the vasomotor tone against rapid changes in arterial pressure or its pulsatile nature, and static autoregulation, involving a rapid response to slow changes in average arterial pressure, mean arterial pressure (MAP). CA can be alternatively tested or monitored by means of different techniques allowing different spatial *versus* temporal resolutions. TCD finds its place halfway in the plot space *versus* time; through the application of different techniques it allows both CA testing or CA monitoring. TCD can test both dynamic and static component of CA. A well-known method for assessing dynamic CA is the 'cuff test'.[56, 57] During this test thigh cuffs are placed on each thigh and tightened from 20 to 50 mmHg above the systolic arterial pressure for 2-3 min and then quickly released, causing a transient blood pressure drop. The dynamic rate of regulation (dROR), whose normal value is 20%, is then calculated from the rate of change in cerebrovascular resistance (MAP/meanFV in MCA) with the blood pressure decreases, basically it indicates how quickly the velocity of cerebral flow returns to its starting level after the hypotensive stimulus. However, potential complications related to the manipulation of systemic arterial pressure in critically ill patients represent a limit to the application of this technique. The transient hyperemic response test (THRT) is another effective test for assessing dynamic cerebral autoregulation. This test is based on the compensatory vasodilatation of the arterioles oc-

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

curring after a brief external compression of the common carotid artery. Intact autoregulation, in order to preserve CBF, react to temporary reduction in CPP with vasodilatation, so as the carotid compression is relieved, a transient increase in blood flow velocity (in the MCA) is observed. Transient hyperemic response ratio (THRR) can be then calculated as the ratio between the velocity of systolic flow during the hyperemic phase and the velocity of basic systolic flow. THRR (Figure 8) is a reliable qualitative autoregulation indicator, however performing a carotid compression with consequent, though transient, reduction in CBF in acute brain injury patients is not always desirable nor safe, therefore performance of THRT should be always carefully evaluated.[58, 59] Regarding dynamic and continuous monitoring of cerebral autoregulatory function, the "mean flow velocity index" (Mx index) is the most commonly used method to assess CA; Mx describes the correlation (coefficient) between CPP and TCD detected mean flow velocity in the MCA: a positive correlation means that blood flow is pressure-dependent indicating a deranged autoregulation, while a negative correlation is observed when autoregulatory function is preserved.[60-62]

Static autoregulation refers to the evaluation of the autoregulatory plateau over a small range of arterial pressure change. Using TCD, MCA FV is measured under normal physiological conditions and then repeated, once a steady state has been reached, following a 20-30 mm Hg increase in mean arterial pressure induced by an hypertensive agent. The index of static autoregulation is calculated as the percent change in the cerebrovascular resistance (calculated as mean arterial pressure/FV) per cent change in the mean arterial pressure. If autoregulation is preserved, FV change should be negligible and the value of the index should be 1. A value of autoregulatory index less than 0.4 suggests impaired autoregulation.[63]

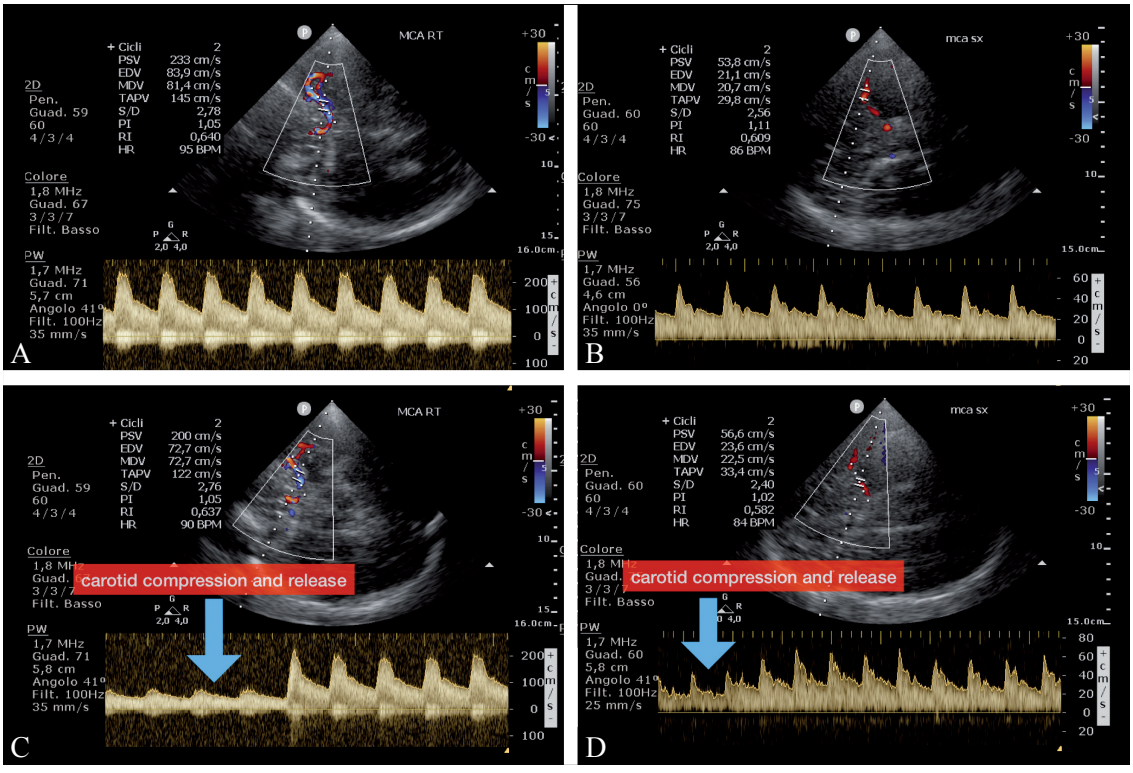

Figure 8.—A-D) Transient hyperemic response test (THRT): after insonation of the right MCA, THRT is performed (lower panels): patient displayed in panel C shows deranged autoregulation at the THRT, while patient displayed in panel D shows preserved autoregulation, in fact after carotid compression and release, CBF acting on a vasodilated vascular bed causes a transient increase in flow velocity.

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

Echography for the assessment of brain anatomy

TCCS has the advantages of being low cost, quick, repeatable, and easily available at the bedside. The main limitation of TCCS is its dependence on adequate temporal acoustic window which is present in 82-95% of patients.[64] On the contrary, patients with skull defects, such as those who have undergone decompressive craniectomy, allow a very accurate assessment of brain parenchyma by TCCS (Figure 9). Results of a recent study showed that in patients with decompressive craniectomy TCCS was as effective as CT scan in assessing hyperdense focal lesions, midline structures shift, ventricular system dimensions and to visualize the position of ventricular monitoring catheters.[65] However, it was not able to assess ischemic lesions and had poor agreement with CT to localize hemorrhagic masses after the acute phase. More recently, another study show that using the same technique was possible to assess also the fourth ventricle with a good correlation between TCCS and CT with an excellent intraclass correlation coefficient (0.954).[66] In a recent case report, bedside TCCS was able to visualize hyperechogenic vegetations in a craniotomized patient with ventriculitis, assess the progression of cerebral complications and their evolution over time, as well as effectively monitor the position of the EVD's tip for intrathecal antibiotic therapy.[67]

Finally TCCS resulted has demonstrated also a good correlation with brain CT scan in measuring the MLS and third ventricle width, and an excellent performance in predicting non compressed peri-mesencephalic cisterns and the presence of the sylvian fissure in acute brain injured patients.[68]

Transcranial Doppler cerebral circulatory arrest and brain death

Brain death determination is a clinical diagnosis, although in certain circumstances ancillary tests are necessary and in some countries mandatory.[69, 70] TCD could be used as a confirmatory test because it can prove cerebral circulatory arrest (CCA), which has distinctive flow patterns including oscillatory flow representing reversal of diastolic flow and systolic spikes representing lack of net forward flow.[71, 72] A recent meta-analysis demonstrated that TCD is highly accurate for brain death confirmation with a sensitivity and specificity of 90% and 98%, respectively.[73] Although TCD has been recommended by medical councils as one of the methods that can support and shorten the waiting time for fulfilling the criteria for Brian Death diagnosis, it evaluates CCA rather than brain stem function, and

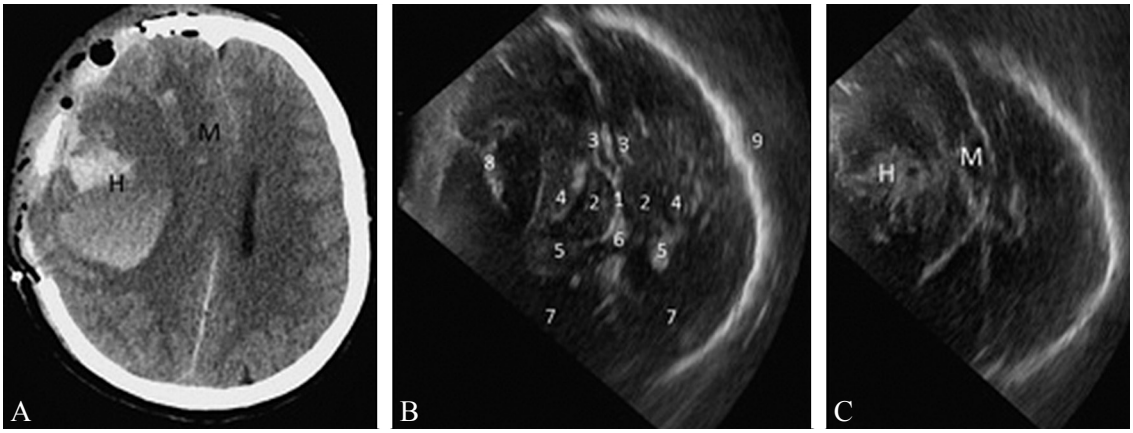

Figure 9.—A-C) Secondary hematoma following Posterior communicating artery (AcoP) aneurysm. Seventy-one years old female who underwent coiling for an AcoP aneurysm and right decompression. A) To be noted a subsequent large hematoma at CT scan (H) which causes a compression of right ventricle and an initial midline shift (M); C) it is well visible at 2 MHz B-mode eco (M and H); B) it was possible to note the well definite basal ganglia structures.
1: third ventricle; 2: thalamus; 3: frontal horn lateral ventricle; 4: posterior limb internal capsule; 5: choroid plexus; 6: splenium of corpus callosum; 7: occipital lobe; 8: lateral sulcus; 9: contralateral skull.

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

this last limitation needs to be taken into account. Finally, trans-cervical insonation of the extracranial ICA and VA with cervical color Doppler ultrasound (CCD) can detect complete CCA. Although CCD is not yet considered valid as an ancillary test, a recent study showed a sensitivity of 78% (96/123 patients) in detecting CCA compared to standard ancillary tests, increasing the sensitivity of TCD by 18% in patients without adequate bone windows at TCD.[73-75]

Conclusions

The noninvasive nature of TCD/TCCS enables the easy and bedside application of this technique in several clinical contexts, allowing the assessment of anatomical structures and cerebrovascular function. Although the high potential of this technique, its use in the daily clinical practice is still poor, and its application needs further validation.

Key messages

- Brain ultrasound allows indirect evaluation of intracranial pressure (ICP) based on different techniques: flow velocity waveform analysis, optic nerve sheath diameter, midline shift assessment.
- Introduction of ultrasound-based techniques for the estimation of ICP in the Focused Assessment Sonography for Trauma is very promising.
- Angiographic vasospasm and delayed cerebral ischemia are the most severe consequences in aSAH patients: reliability of TCD ultrasonography in comparison with DSA is greatest in the M1 segment of the middle cerebral artery (MCA) for detection of vasospasm.
- Cerebral autoregulation (CA) is the ability of the brain to maintain CBF constant despite changes in CPP: TCD allows evaluation of both static and dynamic components of CA: THRT, cuff test and Mx allow evaluation of dynamic component of CA; static component is studied through the assessment of the index of autoregulation.
- TCD/TCCS can be used as a confirmatory test in the assessment of brain death: oscillatory reverse flow, systolic spikes, absence of flow are TCD/TCCS patterns probatory of cerebral circulatory arrest.

References

1. Dussik KT. On the possibility of using ultrasound waves as a diagnostic aid. Neurol Psychiat 1942;174:153-68.

2. Guttner W, Fiedler G, Patzold J. Uber Ultraschallabbildungen am menschlichen Schadel. Acustica 1952;2:148.

3. Babcock DS, Han BK, LeQuesne GW. B-mode gray scale ultrasound of the head in the newborn and young infant. AJR Am J Roentgenol 1980;134:457–68.

4. Aaslid R, Markwalder TM, Nornes H. Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. J Neurosurg 1982;57:769–74.

5. Furuhata H. New evolution of transcranial tomography (TCT) and transcranial color Doppler tomography (TCDT). Neurosonology 1989;2:8–15.

6. Bartels E, Bartels S, Poppert H, editors. New Trends in Neurosonology and Cerebral Hemodynamics — an Update. Perspectives in Medicine 2012. Munich, Germany: Elsevier; 2012.

7. Robba C, Cardim D, Tajsic T, Pietersen J, Bulman M, Rasulo F, *et al.* Non-invasive Intracranial Pressure Assessment in Brain Injured Patients Using Ultrasound-Based Methods. Acta Neurochir Suppl (Wien) 2018;126:69–73.

8. Robba C, Goffi A, Geeraerts T, Cardim D, Via G, Czosnyka M, *et al.* Brain ultrasonography: methodology, basic and advanced principles and clinical applications. A narrative review. Intensive Care Med 2019;45:913–27.

9. Lindegaard KF, Nornes H, Bakke SJ, Sorteberg W, Nakstad P. Cerebral vasospasm diagnosis by means of angiography and blood velocity measurements. Acta Neurochir (Wien) 1989;100:12–24.

10. Ringelstein EB, Kahlscheuer B, Niggemeyer E, Otis SM. Transcranial Doppler sonography: anatomical landmarks and normal velocity values. Ultrasound Med Biol 1990;16:745–61.

11. Martin PJ, Evans DH, Naylor AR. Measurement of blood flow velocity in the basal cerebral circulation: advantages of transcranial color-coded sonography over conventional transcranial Doppler. J Clin Ultrasound 1995;23:21–6.

12. Krejza J, Mariak Z, Babikian VL. Importance of angle correction in the measurement of blood flow velocity with transcranial Doppler sonography. AJNR Am J Neuroradiol 2001;22:1743–7.

13. Manno EM. Transcranial Doppler ultrasonography in the neurocritical care unit. Crit Care Clin 1997;13:79–104.

14. Eicke BM, Tegeler CH, Dalley G, Myers LG. Angle correction in transcranial Doppler sonography. J Neuroimaging 1994;4:29–33.

15. Klingelhöfer J, Conrad B, Benecke R, Sander D, Markakis E. Evaluation of intracranial pressure from transcranial Doppler studies in cerebral disease. J Neurol 1988;235:159–62.

16. Klingelhöfer J, Conrad B, Benecke R, Sander D. Intra-

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

cranial flow patterns at increasing intracranial pressure. Klin Wochenschr 1987;65:542–5.

17. Bellner J, Romner B, Reinstrup P, Kristiansson KA, Ryding E, Brandt L. Transcranial Doppler sonography pulsatility index (PI) reflects intracranial pressure (ICP). Surg Neurol 2004;62:45–51, discussion 51.

18. Behrens A, Lenfeldt N, Ambarki K, Malm J, Eklund A, Koskinen LO. Transcranial Doppler pulsatility index: not an accurate method to assess intracranial pressure. Neurosurgery 2010;66:1050–7.

19. Zweifel C, Czosnyka M, Carrera E, de Riva N, Pickard JD, Smielewski P. Reliability of the blood flow velocity pulsatility index for assessment of intracranial and cerebral perfusion pressures in head-injured patients. Neurosurgery 2012;71:853–61.

20. Bouzat P, Almeras L, Manhes P, Sanders L, Levrat A, David JS, *et al.*; TBI-TCD Study Investigators. Transcranial Doppler to Predict Neurologic Outcome after Mild to Moderate Traumatic Brain Injury. Anesthesiology 2016;125:346–54.

21. Aaslid R. Intracranial pressure IV. New York: Springer, 1986. p. 226–9.

22. Czosnyka M, Matta BF, Smielewski P, Kirkpatrick PJ, Pickard JD. Cerebral perfusion pressure in head-injured patients: a noninvasive assessment using transcranial Doppler ultrasonography. J Neurosurg 1998;88:802–8.

23. Rasulo FA, Bertuetti R, Robba C, Lusenti F, Cantoni A, Bernini M, *et al.* The accuracy of transcranial Doppler in excluding intracranial hypertension following acute brain injury: a multicenter prospective pilot study. Crit Care 2017;21:44.

24. Schmidt B, Klingelhöfer J, Schwarze JJ, Sander D, Wittich I, Wittich I. Noninvasive prediction of intracranial pressure curves using transcranial Doppler ultrasonography and blood pressure curves. Stroke 1997;28:2465–72.

25. Schmidt B, Czosnyka M, Klingelhöfer J. Clinical applications of a non-invasive ICP monitoring method. Eur J Ultrasound 2002;16:37–45.

26. Kashif FM, Verghese GC, Novak V, Czosnyka M, Heldt T. Model-based noninvasive estimation of intracranial pressure from cerebral blood flow velocity and arterial pressure. Sci Transl Med 2012;4:129ra44.

27. Robba C, Cardim D, Tajsic T, Pietersen J, Bulman M, Donnelly J, *et al.* Ultrasound non-invasive measurement of intracranial pressure in neurointensive care: A prospective observational study. PLoS Med 2017;14:e1002356.

28. Cardim D, Robba C, Donnelly J, Bohdanowicz M, Schmidt B, Damian M, *et al.* Prospective Study on Noninvasive Assessment of Intracranial Pressure in Traumatic Brain-Injured Patients: Comparison of Four Methods. J Neurotrauma 2016;33:792–802.

29. Robba C, Donnelly J, Bertuetti R, Cardim D, Sekhon MS, Aries M, *et al.* Doppler non-invasive monitoring of ICP in an animal model of acute intracranial hypertension. Neurocrit Care 2015;23:419–26.

30. Schmidt EA, Czosnyka M, Gooskens I, Piechnik SK, Matta BF, Whitfield PC, *et al.* Preliminary experience of the estimation of cerebral perfusion pressure using transcranial Doppler ultrasonography. J Neurol Neurosurg Psychiatry 2001;70:198–204.

31. Schoser BG, Riemenschneider N, Hansen HC. The impact of raised intracranial pressure on cerebral venous hemodynamics: a prospective venous transcranial Doppler ultrasonography study. J Neurosurg 1999;91:744–9.

32. Cardim D, Robba C, Bohdanowicz M, Donnelly J, Cabella B, Liu X, *et al.* Non-invasive Monitoring of Intracranial Pressure Using Transcranial Doppler Ultrasonography: Is It Possible? Neurocrit Care 2016;25:473–91.

33. Valdueza JM, Schultz M, Harms L, Einhäupl KM. Venous transcranial Doppler ultrasound monitoring in acute dural sinus thrombosis. Report of two cases. Stroke 1995;26:1196–9.

34. Schreiber SJ, Stolz E, Valdueza JM. Transcranial ultrasonography of cerebral veins and sinuses. Eur J Ultrasound 2002;16:59–72.

35. Hansen HC, Helmke K. The subarachnoid space surrounding the optic nerves. An ultrasound study of the optic nerve sheath. Surg Radiol Anat 1996;18:323–8.

36. Launey Y, Nesseler N, Le Maguet P, Mallédant Y, Seguin P. Effect of osmotherapy on optic nerve sheath diameter in patients with increased intracranial pressure. J Neurotrauma 2014;31:984–8.

37. Kim JY, Min HG, Ha SI, Jeong HW, Seo H, Kim JU. Dynamic optic nerve sheath diameter responses to short-term hyperventilation measured with sonography in patients under general anesthesia. Korean J Anesthesiol 2014;67:240–5.

38. Soldatos T, Karakitsos D, Chatzimichail K, Papathanasiou M, Gouliamos A, Karabinis A. Optic nerve sonography in the diagnostic evaluation of adult brain injury. Crit Care 2008;12:R67.

39. Robba C, Santori G, Czosnyka M, Corradi F, Bragazzi N, Padayachy L, *et al.* Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. Intensive Care Med 2018;44:1284–94.

40. Motuel J, Biette I, Srairi M, Mrozek S, Kurrek MM, Chaynes P, *et al.* Assessment of brain midline shift using sonography in neurosurgical ICU patients. Crit Care 2014;18:676.

41. Cardim D, Griesdale DE, Ainslie PN, Robba C, Calviello L, Czosnyka M, *et al.* A comparison of non-invasive versus invasive measures of intracranial pressure in hypoxic ischaemic brain injury after cardiac arrest. Resuscitation 2019;137:221–8.

42. Montrief T, Alerhand S, Jewell C, Scott J. Incorporation of Transcranial Doppler into the ED for the neurocritical care patient. Am J Emerg Med 2019;37:1144–52.

43. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, *et al.*; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2018 Update: A Report From the American Heart Association. Circulation 2018;137:e67–492.

44. Macdonald RL. Origins of the Concept of Vasospasm. Stroke 2016;47:e11–5.

45. Kincaid MS, Souter MJ, Treggiari MM, Yanez ND, Moore A, Lam AM. Accuracy of transcranial Doppler ultrasonography and single-photon emission computed tomography in the diagnosis of angiographically demonstrated cerebral vasospasm. J Neurosurg 2009;110:67–72.

46. Lysakowski C, Walder B, Costanza MC, Tramèr MR. Transcranial Doppler versus angiography in patients with vasospasm due to a ruptured cerebral aneurysm: A systematic review. Stroke 2001;32:2292–8.

47. Vora YY, Suarez-Almazor M, Steinke DE, Martin ML, Findlay JM. Role of transcranial Doppler monitoring in the diagnosis of cerebral vasospasm after subarachnoid hemorrhage. Neurosurgery 1999;44:1237–47, discussion 1247–8.

48. Aaslid R, Huber P, Nornes H. Evaluation of cerebrovascular spasm with transcranial Doppler ultrasound. J Neurosurg 1984;60:37–41.

49. Lindegaard KF. The role of transcranial Doppler in the

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.

COPYRIGHT© 2020 EDIZIONI MINERVA MEDICA

management of patients with subarachnoid haemorrhage—a review. Acta Neurochir Suppl (Wien) 1999;72:59–71.

50. Mursch K, Wachter A, Radke K, Buhre W, Al-Sufi S, Munzel U, *et al.* Blood flow velocities in the basal vein after subarachnoid haemorrhage. A prospective study using transcranial duplex sonography. Acta Neurochir (Wien) 2001;143:793–9.

51. Connolly F, Schreiber SJ, Leithner C, Bohner G, Vajkoczy P, Valdueza JM. Assessment of intracranial venous blood flow after subarachnoid hemorrhage: a new approach to diagnose vasospasm with transcranial color-coded duplex sonography. J Neurosurg 2018;129:1136–42.

52. Lang EW, Diehl RR, Mehdorn HM. Cerebral autoregulation testing after aneurysmal subarachnoid hemorrhage: the phase relationship between arterial blood pressure and cerebral blood flow velocity. Crit Care Med 2001;29:158–63.

53. Czosnyka M, Kirkpatrick PJ, Pickard JD. Multimodal monitoring and assessment of cerebral haemodynamic reserve after severe head injury. Cerebrovasc Brain Metab Rev 1996;8:273–95.

54. Xiong L, Liu X, Shang T, Smielewski P, Donnelly J, Guo ZN, *et al.* Impaired cerebral autoregulation: measurement and application to stroke. J Neurol Neurosurg Psychiatry 2017;88:520–31.

55. Budohoski KP, Czosnyka M, Smielewski P, Varsos GV, Kasprowicz M, Brady KM, *et al.* Monitoring Cerebral Autoregulation After Subarachnoid Hemorrhage. Acta Neurochir Suppl (Wien) 2016;122:199–203.

56. Aaslid R, Lindegaard KF, Sorteberg W, Nornes H. Cerebral autoregulation dynamics in humans. Stroke 1989;20:45–52.

57. Giller CA. A bedside test for cerebral autoregulation using transcranial Doppler ultrasound. Acta Neurochir (Wien) 1991;108:7–14.

58. Smielewski P, Czosnyka M, Kirkpatrick P, Pickard JD. Evaluation of the transient hyperemic response test in head-injured patients. J Neurosurg 1997;86:773–8.

59. Cavill G, Simpson EJ, Mahajan RP. Factors affecting assessment of cerebral autoregulation using the transient hyperaemic response test. Br J Anaesth 1998;81:317–21.

60. Ursino M, Giulioni M, Lodi CA. Relationships among cerebral perfusion pressure, autoregulation, and transcranial Doppler waveform: a modeling study. J Neurosurg 1998;89:255–66.

61. Czosnyka M, Smielewski P, Lavinio A, Pickard JD, Panerai R. An assessment of dynamic autoregulation from spontaneous fluctuations of cerebral blood flow velocity: a comparison of two models, index of autoregulation and mean flow index. Anesth Analg 2008;106:234–9.

62. Budohoski KP, Czosnyka M, de Riva N, Smielewski P, Pickard JD, Menon DK, *et al.* The relationship between cerebral blood flow autoregulation and cerebrovascular pressure reactivity after traumatic brain injury. Neurosurgery 2012;71:652–60.

63. Panerai RB. Assessment of cerebral pressure autoregulation in humans—a review of measurement methods. Physiol Meas 1998;19:305–38.

64. Wijnhoud AD, Franckena M, van der Lugt A, Koudstaal PJ, Dippel ED. Inadequate acoustical temporal bone window in patients with a transient ischemic attack or minor stroke: role of skull thickness and bone density. Ultrasound Med Biol 2008;34:923–9.

65. Caricato A, Mignani V, Bocci MG, Pennisi MA, Sandroni C, Tersali A, *et al.* Usefulness of transcranial echography in patients with decompressive craniectomy: a comparison with computed tomography scan. Crit Care Med 2012;40:1745–52.

66. Bendella H, Maegele M, Hartmann A, Spreer J, Rommel N, Lefering R, *et al.* Cerebral Ventricular Dimensions After Decompressive Craniectomy: A Comparison Between Bedside Sonographic Duplex Technique and Cranial Computed Tomography. Neurocrit Care 2017;26:321–9.

67. Robba C, Simonassi F, Ball L, Pelosi P. Transcranial color-coded duplex sonography for bedside monitoring of central nervous system infection as a consequence of decompressive craniectomy after traumatic brain injury. Intensive Care Med 2019;45:1143–4.

68. Oliveira RA, de Oliveira Lima M, Paiva WS, de Sá Malbouisson LM, Teixeira MJ, Bor-Seng-Shu E. Comparison between Brain Computed Tomography Scan and Transcranial Sonography to Evaluate Third Ventricle Width, Peri-Mesencephalic Cistern, and Sylvian Fissure in Traumatic Brain-Injured Patients. Front Neurol 2017;8:44.

69. Wijdicks EF. The diagnosis of brain death. N Engl J Med 2001;344:1215–21.

70. Wijdicks EF. Brain death worldwide: accepted fact but no global consensus in diagnostic criteria. Neurology 2002;58:20–5.

71. Chang JJ, Tsivgoulis G, Katsanos AH, Malkoff MD, Alexandrov AV. Diagnostic Accuracy of Transcranial Doppler for Brain Death Confirmation: Systematic Review and Meta-Analysis. AJNR Am J Neuroradiol 2016;37:408–14.

72. Wahlster S, Wijdicks EF, Patel PV, Greer DM, Hemphill JC 3rd, Carone M, *et al.* Brain death declaration: practices and perceptions worldwide. Neurology 2015;84:1870–9.

73. Escudero D, Valentín MO, Escalante JL, Sanmartín A, Perez-Basterrechea M, de Gea J, *et al.* Intensive care practices in brain death diagnosis and organ donation. Anaesthesia 2015;70:1130–9.

74. Pardo AV, Cacciatori A, Dorfman B; Consensus Group on Transcranial Doppler in Diagnosis of Brain Death. Latin American consensus on the use of transcranial Doppler in the diagnosis of brain death. Rev Bras Ter Intensiva 2014;26:240–52.

75. Pedicelli A, Bartocci M, Lozupone E, D'Argento F, Alexandre A, Garignano G, *et al.* The role of cervical color Doppler ultrasound in the diagnosis of brain death. Neuroradiology 2019;61:137–45.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

History.—Article first published online: January 8, 2020. - Manuscript accepted: December 12, 2019. - Manuscript revised: November 6, 2019. - Manuscript received: May 5, 2019.

This document is protected by international copyright laws. No additional reproduction is authorized. It is permitted for personal use to download and save only one file and print only one copy of this Article. It is not permitted to make additional copies (either sporadically or systematically, either printed or electronic) of the Article for any purpose. It is not permitted to distribute the electronic copy of the article through online internet and/or intranet file sharing systems, electronic mailing or any other means which may allow access to the Article. The use of all or any part of the Article for any Commercial Use is not permitted. The creation of derivative works from the Article is not permitted. The production of reprints for personal or commercial use is not permitted. It is not permitted to remove, cover, overlay, obscure, block, or change any copyright notices or terms of use which the Publisher may post on the Article. It is not permitted to frame or use framing techniques to enclose any trademark, logo, or other proprietary information of the Publisher.